AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1. (Currently amended) A method of performing targeted modifications of human embryonic stem (ES) cells, the method comprising the steps of;

electroporating copies of a genetic construct into clumps of human ES cells in a culture medium, wherein the construct comprises a marker gene for cellular identification ~~on an insert~~ flanked by 3' and 5' arms homologous to genomic regions that flank an insertion site in ~~an ES cell genome~~ the ES cell genomes, so that homologous recombination occurs between the 3' and 5' arms and the ~~stem~~ ES cell genomic regions; and

identifying cells that contain the marker gene.

2. (Cancelled)

3. (Currently amended) [[A]] The method ~~as claimed in~~ of claim 1, wherein ~~upon recombination,~~ the construct does not comprise a promoter operably linked to the marker and wherein, following recombination, cells in a desired state of differentiation that express the marker gene are isolated ~~is operably linked with a differentiation-specific promoter in the genome such that the marker gene is expressed only in cells in a desired state of differentiation~~.

4. (Currently amended) [[A]] The method ~~as claimed in~~ of claim 1 wherein the genetic construct includes a tissue-specific promoter that drives expression of the marker gene only in cells in a desired state of differentiation.

5. (Withdrawn) Human cells in culture derived from human embryonic stem cells, the cells comprising in their genome an inserted genetic construct which knocks out the functioning of a gene which would otherwise be expressed in those human cells in culture.

6. (Withdrawn) Human cells in culture derived from human embryonic stem cells, the cells comprising in their genome an inserted genetic construct which introduced a mutation into a native gene in those human cells in culture.

7. (Currently amended) A method of purifying cells of a defined lineage from a culture of human ~~embryonic stem (~~ES~~)~~ cells, the method comprising the steps of;

(a) electroporating copies of a genetic construct into clumps of human ES cells in a culture medium, the genetic construct comprising ~~an insert having~~ a marker gene expressed only in the defined lineage cells, the ~~insert~~ marker gene flanked by 3' and 5' arms homologous to genomic regions that flank an insertion site in ~~an ES cell genome~~ the ES cell genomes so that homologous recombination occurs between the 3' and 5' arms and the ~~stem~~ ES cell genomic regions;

(b) identifying cells that express the marker gene; and

(c) purifying the cells expressing the marker gene from cells not expressing the marker gene.

8. (Currently amended) [[A]] The method ~~as claimed in~~ of claim 7 wherein the marker gene is operably linked to a promoter active only in the defined lineage cells.

9. (Currently amended) [[A]] The method ~~as claimed in~~ of claim 7 wherein after the electroporating step, the ES cells are permitted to differentiate.

10. (Currently amended) [[A]] The method ~~as claimed in~~ of claim 7 wherein the marker gene encodes a fluorescent gene product and the identifying and purifying is performed by fluorescence activated cell sorting.

11. (Withdrawn) A culture of differentiated human cells derived from human ES cells and purified by the method of claim 7 for cells of a desired lineage.

12. (Currently amended) A method for purifying differentiated cells ~~of a defined lineage~~ obtained from human ~~embryonic stem (ES)~~ cells, the method comprising the steps of

a) identifying expressed genes characteristic of defined lineage cells purified by a method of Claim 7;

b) culturing non-transformed human ES cells under differentiating conditions to yield a culture that comprises differentiated cells; and

c) purifying ~~defined lineage~~ differentiated cells that express the characteristic genes from the culture that comprises differentiated cells.

13. (Cancelled)

14. (Withdrawn) Human cells in culture derived from human embryonic stem cells, the cells comprising in their genome an inserted genetic construct which expresses an inserted gene only when the human cells are in a desired state of differentiation.

15. (Withdrawn) Human cells in culture as claimed in claim 14 wherein the desired state of differentiation is an undifferentiated state.

16. (Withdrawn) Human cells in culture as claimed in claim 14 where the gene is a marker gene the expression of which can be observed visually.

17. (Currently amended) A method of performing targeted modifications of human ~~embryonic stem (ES)~~ cells, the method comprising the steps of

a) electroporating copies of a genetic construct into clumps of human ES cells in a culture medium, wherein the construct comprises a foreign gene and a marker gene flanked by 3' and 5' arms homologous to genomic regions flanking an insertion site in ~~an ES cell genome~~ the ES cell genomes, so that homologous recombination occurs between the 3' and 5' arms and the ~~stem~~ ES cell genomic regions,

(i) wherein the marker gene comprises a promoter active in cells of a defined lineage, or

(ii) wherein in the absence of a promoter, the construct is designed to recombine with the selected regions of the ES cell genomes, such that the marker gene is operably linked to an endogenous, tissue specific promoter; and

b) identifying cells that express the marker gene.

18. (Previously presented) The method of claim 17, further comprising purifying the cells of step b) expressing the marker from cells not expressing the marker, wherein the cells expressing the marker are of a defined lineage.

19. (Currently amended) The method of claim 1, wherein ~~copies of the genetic construct are electroporated into human ES cells with~~ a single 320 volt, 200 microfarad pulse is used for electroporation.

20. (Currently amended) The method of claim 7, wherein ~~copies of the genetic construct are electroporated into human ES cells with~~ a single 320 volt, 200 microfarad pulse is used for electroporation.

21. (Currently amended) The method of claim 17, wherein ~~copies of the genetic construct are electroporated into human ES cells with~~ a single 320 volt, 200 microfarad pulse is used for electroporation.